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RESEARCH LETTER

Intramolecular C–H insertion catalyzed by dirhodium(II) complexes using CO_2 as the reaction media

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In this work, the intramolecular C–H insertion of diazoacetamides catalyzed by dirhodium(II) complexes and using CO_2 as solvent is disclosed. The expected lactams were obtained in yields over 97%. The asymmetric intramolecular C–H insertion was also achieved and the β-lactam 14 was obtained in >97% yield and 65% *ee* using the chiral dirhodium(II) catalyst Rh_2(*S*-PTTL)$_4$. Finally, the dirhodium(II) complex $Rh_2(OAc)_4$ was used in two consecutive cycles in which complete conversion to the lactam was observed.

Keywords: diazoacetamides; C–H insertion; dirhodium(II); lactams; $scCO_2$

Introduction

The C–H insertion reaction of diazo compounds catalyzed by dirhodium(II) complexes has developed in to a very reliable methodology to form new C–C bonds from otherwise unreactive C–H bonds. As shown in Scheme 1, this reaction involves the generation of a metallocarbene that undergoes the C–H insertion forming the new C–C bond and at the same time that regenerates the catalyst (*1–8*).

From the sustainability point of view, the catalyzed C–H bond insertion starting from diazo compounds is an ideal process as it affords important C–C bonds generating nitrogen as the sole waste if only the C–H insertion step is considered. In order to further improve the sustainability of this methodology, it is important to introduce more benign reaction media as the reaction is typically carried out in organic solvents such as dichloromethane in order to avoid catalyst inhibition due to solvent coordination onto the complex axial positions (Scheme 1) (*1–8*). In addition to this, dirhodium(II) complexes are quite expensive and for that reason methodologies that enable the catalyst recycling are of pivotal importance(*9–20*). Over the years, we have been particularly interested on developing methods to perform the catalyst reutilization and on the study of new solvents to perform this reaction. In this field, we established ionic liquids as the reaction media in which the catalyst reutilization was achieved in six cycles, and we discovered that water could also be very efficiently used as a solvent allowing the catalyst reutilization ($Rh_2(OAc)_4$) in over 11 cycles (*21–25*). Despite the usefulness of these approaches, both required the product extraction using organic solvents and product purification. Taking this into consideration, we conceived that an ideal methodology would involve the reaction taking place in a solvent that affords the product in high yields and at the same time that enables the product/catalyst separation, leaving the complex ready for another reaction cycle. Considering the aforementioned requirements, we envisioned that supercritical CO_2 ($scCO_2$) could be the solvent of choice for this process.

Experimental

General procedure for the cyclization of diazoacetamide with dirhodium(II) complexes in CO_2: A 3.5-mL high-pressure cell was charged with diazoacetamide (0.173 mmol) and dirhodium(II) complex (1 mol%) and placed inside a constant temperature water bath. CO_2 was introduced into the cell by a screw injector pump, at a constant temperature of 30°C. The mixture was stirred with a magnetic stirrer for 24 hours under 30°C and 70 bar. After which, the system was depressurized and the product was filtered

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